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N-Ac-Sar-Gly-Val-D-Ile-Thr-Gln-Ile-Arg-ProNHCH₂CH₃, or a pharmaceutically acceptable salt, ester, solvate, or prodrug thereof, and a pharmaceutically acceptable carrier.

32 (New). A composition for the treatment of a disease selected from cancer, arthritis, psoriasis, angiogenesis of the eye associated with infection or surgical intervention, macular degeneration, and diabetic retinopathy comprising N-Ac-Sar-Gly-Val-D-alloIle-Ser-Ser-Ile-Arg-ProNHCH₂CH₃, or a pharmaceutically acceptable salt, ester, solvate, or prodrug thereof and a pharmaceutically acceptable carrier.

REMARKS

Claims 1-17 were pending in the subject application. After entry of this amendment, claims 1-14, 16, and 18-32 will be pending.

The amendment accompanying these remarks cancels claims 15 and 17 as being outside the scope of elected Group 1 and amends claim 1 to recite the amino acyl residue "glycyl" as option (13) under A₂, to remove variables in claim 1 which are outside the scope of Group 1, and to correct a minor typographical error.

Support for the recitation of glycyl in claim 1 is found on page 19, lines 15-19 and in Examples 1-152, 161-334, 337 (in part), 339 (in part), and 340-356 in the specification.

CONCLUSION

This amendment addresses the issues raised in the Official action and places the claims in condition for allowance. Entry of the proposed amendment and allowance of Claims 1-14, 16, and 18-32 is respectfully requested.



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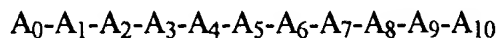
ABBOTT LABORATORIES
Telephone: (847) 937-3810
Facsimile: (847) 938-2623

Respectfully submitted,
J. Henkin, et al.

B. Gregory Donner
Registration No. 34,580
Attorney for Applicants

VERSION OF CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

1 (Amended). A compound of the formula:



or a pharmaceutically acceptable salt, ester, solvate or prodrug thereof, wherein:

A₀ is **[hydrogen or]** an acyl group selected from:

- (1) R-(CH₂)_n-C(O)-; wherein n is an integer from 0 to 8 and R is selected from hydroxyl; methyl; N-acetylamino; methoxyl; carboxyl; cyclohexyl optionally containing a one or two double bonds and optionally substituted with one to three hydroxyl groups; and a 5- or 6-membered ring aromatic or nonaromatic ring optionally containing one or two heteroatoms selected from nitrogen, oxygen, and sulfur, wherein the ring is optionally substituted with a moiety selected from alkyl, alkoxy, and halogen; and
- (2) R¹-CH₂CH₂-(OCH₂CH₂O)_p-CH₂-C(O)-; wherein R¹ is selected from hydrogen, alkyl, and N-acetylamino, and p is an integer from 1 to 8;

A₁ is an amino acyl residue selected from:

- (1) alanyl,
- (2) asparaginylyl,
- (3) citrullyl,
- (4) glutaminylyl,
- (5) glutamyl,
- (6) N-ethylglycyl,
- (7) methionyl,
- (8) N-methylalanyl,
- (9) prolyl,
- (10) pyro-glutamyl,
- (11) sarcosyl,
- (12) seryl,

- (13) threonyl,
- (14) $\text{-HN-(CH}_2\text{)}_q\text{-C(O)-}$, wherein q is 1 to 8, and
- (15) $\text{-HN-CH}_2\text{CH}_2\text{-(OCH}_2\text{CH}_2\text{O)}_r\text{-CH}_2\text{-C(O)-}$, wherein r is 1 to 8;

A₂ is an amino acyl residue selected from:

- (1) alanyl,
- (2) asparaginylyl,
- (3) aspartyl,
- (4) glutaminylyl,
- (5) glutamyl,
- (6) leucyl,
- (7) methionyl,
- (8) phenylalanyl,
- (9) prolyl,
- (10) seryl,
- (11) $\text{-HN-(CH}_2\text{)}_q\text{-C(O)-}$, wherein q is 1 to 8, **[and]**
- (12) $\text{-HN-CH}_2\text{CH}_2\text{-(OCH}_2\text{CH}_2\text{O)}_r\text{-CH}_2\text{-C(O)-}$, wherein r is 1 to 8[;], **and**
- (13) glycyl;**

A₃ is an amino acyl residue selected from:

- (1) alanyl,
- (2) asparaginylyl,
- (3) citrullyl,
- (4) cyclohexylalanyl,
- (5) cyclohexylglycyl,
- (6) glutaminylyl,
- (7) glutamyl,
- (8) glycyl,
- (9) isoleucyl,
- (10) leucyl,
- (11) methionyl,
- (12) norvalyl,
- (13) phenylalanyl,
- (14) seryl,
- (15) *t*-butylglycyl,
- (16) threonyl,

- (17) valyl,
- (18) penicillaminy, and
- (19) cystyl;

A₄ is an amino acyl residue of L or D configuration selected from:

- (1) allo-isoleucyl,
- (2) glycyl,
- (3) isoleucyl,
- (4) prolyl,
- (5) dehydroleucyl,
- (6) D-alanyl,
- (7) D-3-(naphth-1-yl)alanyl,
- (8) D-3-(naphth-2-yl)alanyl,
- (9) D-(3-pyridyl)-alanyl,
- (10) D-2-aminobutyryl,
- (11) D-allo-isoleucyl,
- (12) D-allo-threonyl,
- (13) D-allylglycyl,
- (14) D-asparaginy, and
- (15) D-aspartyl,
- (16) D-benzothienyl,
- (17) D-3-(4,4'-biphenyl)alanyl,
- (18) D-chlorophenylalanyl,
- (19) D-3-(3-trifluoromethylphenyl)alanyl,
- (20) D-3-(3-cyanophenyl)alanyl,
- (21) D-3-(3,4-difluorophenyl)alanyl,
- (22) D-citrullyl,
- (23) D-cyclohexylalanyl,
- (24) D-cyclohexylglycyl,
- (25) D-cystyl,
- (26) D-cystyl(*S-t*-butyl),
- (27) D-glutaminy, and
- (28) D-glutamyl,
- (29) D-histidyl,
- (30) D-homoisoleucyl,

- (31) D-homophenylalanyl,
- (32) D-homoseryl,
- (33) D-isoleucyl,
- (34) D-leucyl,
- (35) D-lysyl(N-epsilon-nicotinyl),
- (36) D-lysyl,
- (37) D-methionyl,
- (38) D-neopentylglycyl,
- (39) D-norleucyl,
- (40) D-norvalyl,
- (41) D-ornithyl,
- (42) D-penicillaminy,
- (43) D-penicillaminy(acetamidomethyl),
- (44) D-penicillaminy(*S*-benzyl),
- (45) D-phenylalanyl,
- (46) D-3-(4-aminophenyl)alanyl,
- (47) D-3-(4-methylphenyl)alanyl,
- (48) D-3-(4-nitrophenyl)alanyl,
- (49) D-3-(3,4-dimethoxyphenyl)alanyl,
- (50) D-3-(3,4,5-trifluorophenyl)alanyl,
- (51) D-prolyl,
- (52) D-seryl,
- (53) D-seryl(*O*-benzyl),
- (54) D-*t*-butylglycyl,
- (55) D-thienylalanyl,
- (56) D-threonyl,
- (57) D-threonyl(*O*-benzyl),
- (58) D-tryptyl,
- (59) D-tyrosyl(*O*-benzyl),
- (60) D-tyrosyl(*O*-ethyl),
- (61) D-tyrosyl, and
- (62) D-valyl;

A₅ is an amino acyl residue of L or D configuration selected from:

- (1) alanyl,

- (2) (3-pyridyl)alanyl,
- (3) 3-(naphth-1-yl)alanyl,
- (4) 3-(naphth-2-yl)alanyl,
- (5) allo-threonyl,
- (6) allylglycyl,
- (7) glutaminy,
- (8) glycyl,
- (9) histidyl,
- (10) homoseryl,
- (11) isoleucyl,
- (12) lysyl(N-epsilon-acetyl),
- (13) methionyl,
- (14) norvalyl,
- (15) octylglycyl,
- (16) ornithyl,
- (17) 3-(4-hydroxymethylphenyl)alanyl,
- (18) prolyl,
- (19) seryl,
- (20) threonyl,
- (21) tryptyl,
- (22) tyrosyl,
- (23) D-allo-threonyl,
- (24) D-homoseryl,
- (25) D-seryl,
- (26) D-threonyl,
- (27) penicillaminy, and
- (28) cystyl;

A₆ is an amino acyl residue of L or D configuration selected from:

- (1) alanyl,
- (2) 3-(naphth-1-yl)alanyl,
- (3) 3-(naphth-2-yl)alanyl,
- (4) (3-pyridyl)alanyl,
- (5) 2-aminobutyryl,
- (6) allylglycyl,

- (7) arginyl,
- (8) asparaginyl,
- (9) aspartyl,
- (10) citrullyl,
- (11) cyclohexylalanyl,
- (12) glutaminyl,
- (13) glutamyl,
- (14) glycyl,
- (15) histidyl,
- (16) homoalanyl,
- (17) homoleucyl,
- (18) homoseryl,
- (19) isoleucyl,
- (20) leucyl,
- (21) lysyl(N-epsilon-acetyl),
- (22) lysyl(N-epsilon-isopropyl),
- (23) methionyl(sulfone),
- (24) methionyl(sulfoxide),
- (25) methionyl,
- (26) norleucyl,
- (27) norvalyl,
- (28) octylglycyl,
- (29) phenylalanyl,
- (30) 3-(4-carboxyamidophenyl)alanyl,
- (31) propargylglycyl,
- (32) seryl,
- (33) threonyl,
- (34) tryptyl,
- (35) tyrosyl,
- (36) valyl,
- (37) D-3-(naphth-1-yl)alanyl,
- (38) D-3-(naphth-2-yl)alanyl,
- (39) D-glutaminyl,
- (40) D-homoseryl,

- (41) D-leucyl,
- (42) D-norvalyl,
- (43) D-seryl,
- (44) penicillaminy, and
- (45) cystyl;

A₇ is an amino acyl residue of L or D configuration selected from:

- (1) alanyl,
- (2) allylglycyl,
- (3) aspartyl,
- (4) citrullyl,
- (5) cyclohexylglycyl,
- (6) glutamyl,
- (7) glycyl,
- (8) homoseryl,
- (9) isoleucyl,
- (10) allo-isoleucyl
- (11) leucyl,
- (12) lysyl(N-epsilon-acetyl),
- (13) methionyl,
- (14) 3-(naphth-1-yl)alanyl,
- (15) 3-(naphth-2-yl)alanyl,
- (16) norvalyl,
- (17) phenylalanyl,
- (18) prolyl,
- (19) seryl,
- (20) *t*-butylglycyl,
- (21) tryptyl,
- (22) tyrosyl,
- (23) valyl,
- (24) D-allo-isoleucyl,
- (25) D-isoleucyl,
- (26) penicillaminy, and
- (27) cystyl;

A₈ is an amino acyl residue selected from:

- (1) 2-amino-4-[(2-amino)-pyrimidinyl]butanoyl,
- (2) alanyl(3-guanidino),
- (3) alanyl[3-pyrrolidinyl(2-N-amidino)],
- (4) alanyl[4-piperidinyl(N-amidino)],
- (5) arginyl,
- (6) arginyl(N^GN^{G'}diethyl),
- (7) citrullyl,
- (8) 3-(cyclohexyl)alanyl(4-N¹-isopropyl),
- (9) glycyl[4-piperidinyl(N-amidino)],
- (10) histidyl,
- (11) homoarginyl,
- (12) lysyl,
- (13) lysyl(N-epsilon-isopropyl),
- (14) lysyl(N-epsilon-nicotinyl),
- (15) norarginyl,
- (16) ornithyl(N-delta-isopropyl),
- (17) ornithyl(N-delta-nicotinyl),
- (18) ornithyl[N-delta-(2-imidazoliny)],
- (19) [(4-amino(N-isopropyl)methyl)phenyl]alanyl,
- (20) 3-(4-guanidinophenyl)alanyl, and
- (21) 3-(4-amino-N-isopropylphenyl)alanyl;

A₉ is an amino acyl residue of L or D configuration selected from:

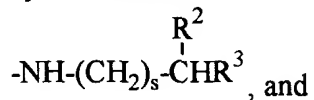
- (1) 2-amino-butyryl,
- (2) 2-amino-isobutyryl,
- (3) homoprolyl,
- (4) hydroxyprolyl,
- (5) isoleucyl,
- (6) leucyl,
- (7) phenylalanyl,
- (8) prolyl,
- (9) seryl,
- (10) *t*-butylglycyl,
- (11) 1,2,3,4-tetrahydroisoquinoline-3-carbonyl,
- (12) threonyl,

- (13) valyl,
- (14) D-alanyl, and
- (15) D-prolyl; and

A₁₀ is a hydroxyl group or an amino acid amide is selected from:

azaglycylamide,
 D-alanylamine,
 D-alanylethylamine,
 glycylamide,
 glycylethylamine,
 sarcosylamine,
 serylamine,
 D-serylamine,

a group represented by the formula



a group represented by the formula $-\text{NH}-\text{R}^4$;

wherein:

s is an integer selected from 0 to 8,

R² is selected from hydrogen, alkyl, and a 5- to 6-membered cycloalkyl ring;

R³ is selected from hydrogen, hydroxy, alkyl, phenyl, alkoxy, and a 5- to 6-membered ring optionally containing from one to two heteroatoms selected from oxygen, nitrogen, and sulfur, provided that s is not zero when R³ is hydroxy or alkoxy; and

R⁴ is selected from hydrogen, hydroxy, and a 5- to 6-membered cycloalkyl ring.